Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (Currently Amended): A method for the identification of aberrant phenotypes expressed by neoplastic cells comprising the steps of:

a) separately staining one or more normal/reactive samples and one neoplastic sample with overlapping multiple combinations of monoclonal antibodies, each monoclonal antibody in each combination being conjugated to a different fluorochrome and each combination having in common at least three fluorochrome conjugated monoclonal antibodies that are specific for tumor cells of interest contained in said neoplastic samples;

b) sequentially measuring at least two light scatter emissions and the at least four fluorescence emissions ~~associated to large numbers of cells stained with each of the combinations of monoclonal antibodies~~ of each stained cell from the normal/reactive samples and the neoplastic sample, using flow

cytometry;

c) storing two independent list mode data files, one containing measurement information on the specific light scatter and fluorescence characteristics of each cell analyzed from the normal/reactive samples in step b) and the other containing measurement information on the specific light scatter and fluorescence characteristics of each cell analyzed from the neoplastic sample in step b);

d) creating new data files from step c) by merging, at known proportions cellular events from the data file containing measurement information about the cells present in the neoplastic sample from step b) into the data file containing measurement information on the cells present in the normal/reactive samples from step b);

e) defining in a multidimensional space generated by the flow cytometric measurements of light scatter and fluorescence emissions from preestablished standards, those areas occupied by events corresponding to normal cells and those areas corresponding to empty spaces in normal/reactive samples and that

may be occupied by tumor cells in neoplastic samples;

f) sequentially identifying in the data files containing measurement information about the cells present in the neoplastic sample and merged as described in step d), those events corresponding to neoplastic cells as those populations of events contained in the neoplastic sample which fall into the empty spaces identified in the multidimensional space generated by the flow cytometric measurements of light scatter and fluorescence emissions from pre-established standards in step e); and

g) establishing and identifying the phenotypic aberrations displayed by the neoplastic cells as compared to their normal counterpart, as those combinations of flow cytometric measurements of light scatter and fluorescence emissions from the events corresponding to the neoplastic cells contained in the merged data file from step d), that provide their identification and distinction from those events corresponding to cells from normal/reactive samples contained in the same merged data file from step d).

Claim 2 (Original): The method of claim 1, wherein the samples comprise peripheral blood.

Claim 3 (Original): The method of claim 1, wherein the samples comprise bone marrow.

Claim 4 (Original): The method of claim 1, wherein the samples comprise spinal fluid.

Claim 5 (Original): The method of claim 1, wherein the samples comprise lymph node.

Claim 6 (Original): The method of claim 1, wherein more than one randomly selected normal sample is stained.

Claim 7 (Original): The method of claim 1, wherein more than one normal sample is stained, all normal samples being selected from a well defined age group of individuals, or from any other group of individuals defined according to their gender and underlying non-neoplastic conditions.

Claim 8 (Original): The method of claim 1, wherein the neoplastic samples contain hematopoietic tumor cells of one or more different types.

Claim 9 (Original): The method of claim 1, wherein the

neoplastic samples contain non-hematopoietic tumor cells of one or more different types.

Claim 10 (Original): The method of claim 1, wherein the neoplastic samples contain both hematopoietic neoplastic cells and non-hematopoietic tumor cells.

Claim 11 (Original): The method of claim 1, wherein the neoplastic samples are obtained at first diagnosis, relapse and at any time period after diagnosis.

Clam 12 (Original): The method of claim 1, wherein the neoplastic samples may contain high or minimal numbers of neoplastic cells.

Claim 13 (Previously Presented): The method of claims 1, wherein the samples are stained ex vivo, directly at blood collection.

Claim 14 (Original): The method of claim 1, wherein the samples are stained after being cultured in vitro.

Claim 15 (Original): The method of claim 1, wherein the

panels of multiple combinations of monoclonal antibodies used to stain neoplastic samples and normal/reactive samples are identical.

Claim 16 (Previously Presented): The method of claim 1, wherein the panel of multiple combinations of monoclonal antibodies that is contacted to the neoplastic samples is in consonance for each labeled monoclonal antibody contained in said combinations of monoclonal antibodies, with the panel of combinations of monoclonal antibodies used to stain the normal/reactive samples, but with the inclusion of more labeled monoclonal antibodies into the cocktail that is subjected to contact with the normal/reactive samples.

Claim 17 (Original): The method of claim 1, wherein for each pair of panels of combinations of monoclonal antibodies, an exact clone of each monoclonal antibody used in each individual combination of monoclonal antibodies, and a fluorochrome to which it is conjugated, are identical in the two panels of combinations of monoclonal antibodies.

Claim 18 (Previously Presented): The method of claim 1, wherein the number of labeled monoclonal antibodies contained in

each combination is composed of four or more different labeled monoclonal antibody reagents.

Claim 19 (Previously Presented): The method of claim 1, wherein the number of labeled monoclonal antibody reagents in common for all said combinations, is of three or more different labeled monoclonal antibodies.

Claim 20 (Original): The method of claim 1, wherein the exact monoclonal antibodies that are common to all combinations of monoclonal antibodies used in a panel to stain a pair of normal/reactive samples and a neoplastic sample may vary depending on the type, the lineage and the maturation stage of the tumor cells contained in the neoplastic sample.

Claim 21 (Original): The method of claim 1, wherein at least four different fluorochromes are used, each being conjugated to a different monoclonal antibody, a fluorescence emission of each fluorochrome being distinguishable from that of the other fluorochrome-conjugated monoclonal antibodies.

Claim 22 (Previously Presented): The method of claim 21, wherein a combination of fluorochromes is selected from the group

consisting of fluorescein isothiocyanate (FITC), phycoerythrin (PE), peridin chlorophyll protein (PerCP), allophycocyanin, ALEXA FLUOR 488®, ALEXA 647®, pacific blue, ALEXA FLOUR 405®, cyanin 5 (Cy5), cyanin5.5(Cy5.5) and conjugates thereof coupled to PE, to APC or to PerCP (PE/Cy5, PE/Cy5.5, PE/Cy7, APC/Cy7 and PerCP/Cy5.5) and any additional fluorochrome.

Claims 23-24 (Canceled).

Claim 25 (Original): The method of claim 1, wherein information from two distinct data files is merged directly without any correction.

Claim 26 (Original): The method of claim 1, wherein information from two different data files is merged after adjusting a relative position of populations of cellular events measured according to pre-established standards.

Claim 27 (Original): The method of claim 1, wherein the pre-established standards are reference microparticles.

Claim 28 (Original): The method of claim 27, wherein population of reference microparticles is uniform.

Claim 29 (Original): The method of claim 27, wherein a population of reference microparticles is composed of multiple populations of microbeads of differing size, density, volume, shape, amount of fluorescence, adhesion characteristics or other physico-chemical properties.

Claim 30 (Original): The method of claim 27, wherein a population of microparticles is composed of fluorescent particles.

Claim 31 (Previously Presented): The method of claim 27, wherein a population of microparticles is composed of microparticles that have anti-immunoglobulin antibodies coated or immobilized on their surface.

Claim 32 (Previously Presented): The method of claim 27, wherein a population of microparticles is that have anti-immunoglobulin antibodies coated or immobilized on their surface.

Claim 33 (Original): The method of claim 27, wherein the microparticles are added in known numbers.

Claim 34 (Previously Presented): The method of claim 27,

wherein serial dilutions of events from a data file corresponding to a neoplastic sample stained with a panel of monoclonal antibody combinations into a data file containing information on the light scatter and fluorescence measures of cells contained in one or more normal/reactive samples stained with an identical panel of monoclonal antibodies, are made to evaluate the sensitivity at which a small number of events corresponding to neoplastic cells could be detected once diluted at predefined known proportions with cellular events from a data file corresponding to a normal/reactive sample.

Claim 35 (Canceled).